Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims

1. (Previously Presented) A compound having the formula

$(X - Y_m)_n$- S,

wherein

X is a pharmaceutically active compound,

Y is a bifunctional linker,

S is a mono-, di- or trisaccharide

n is equal or less than the number of the saccharide units in S, and

m is, independently of n, 0 or 1,

and wherein at least one saccharide unit of S is derived from an aldose monosaccharide comprising a free aldehyde group.

2. (Previously Presented) The compound of claim 1, wherein m = 0, and X and S are linked to each other by an amide, imine, secondary or tertiary amine, ether, ester, carbonate, carbamate, urea or thioester bond.

3. (Previously Presented) The compound of claim 1, wherein m = 1, and X and S are linked by means of a pharmaceutical acceptable linking group, said linking group preferably being linked to X and S by an amide, imine, secondary or tertiary amine, ether, ester, carbonate, carbamate, urea or thioester bond and wherein the X-Y bond may be different from the Y-S bond.

4. (Currently Amended) The compound of ~~any one of claims 1 to 3~~ claim 1, wherein S is linear and the saccharide ~~unit(s)~~ units within S are linked by α(1-4) bonds.

5. (Currently Amended) The compound of ~~any one of claims 1 to 4~~ claim 1, wherein the viscosity of said compound is 1-100 mPasc~~, preferably 1-10 mPasc, more preferably 1-7 mPase~~.

6. (Currently Amended) The compound of ~~any one of claims 1 to 4~~ claim 1, wherein the molar ratio of X to S is in the range of 20:1 to 1:1~~, preferably in the range of 15:1 to 1:1, more preferably in the range of 5:1 to 1:1, most preferably about 1:1~~.

7. (Currently Amended) The compound of ~~any one of claims 1 to 5~~ claim 1, wherein S comprises one or more ~~of the oligosaccharide unit (s) which is (are) identical or different and each~~ saccharide units selected from the group consisting of:

~~h)~~ monosaccharides, ~~preferably: ribose, arabinose, xylose, lyxose, allose, altrose, glucose, mannose, gulose, idose, galactose, talose, fucose;~~

~~i)~~ disaccharides, ~~preferably lactose, maltose, isomaltose, cellobiose, gentiobiose, melibiose, primeverose, rutinose;~~

~~j)~~ disaccharide homologues, ~~preferably maltotriose, isomaltotriose, lactotriose;~~

~~k) uronic acids, preferably glucuronic acid, galacturonic acid;~~

~~l)~~ branched oligosaccharides, ~~preferably panose, isopanose,~~

~~m)~~ amino monosaccharides, ~~preferably galactosamine, glucosamine, mannosamine, fucosamine, quinovosamine, neuraminic acid, muramic acid; lactosediamine, acosamine, bacillosamine, daunosamine, desosamine, forosamine, garosamine, kanosamine, kansosamine, mycaminose, mycosamine, perosamine, pneumosamine, purpurosamine, rhodosamine;~~ and

~~n)~~ modified saccharides~~, preferably abequose, amicetose, arcanose, ascarylose, boivinose, chacotriose, chalcose, cladinose, colitose, cymarose, 2-deoxyribose, 2-deoxyglucose, diginose, digitalose, digitoxose, evalose, evernitrose, hamamelose, manninotriose, melibiose, mycarose, mycinose, nigerose, noviose, oleandrose, paratose, rhodinose, rutinose, sarmentose, sedoheptulose, solatriose, sophorose, streptose, turanose, tyvelose~~.

8. (Currently Amended) The compound of claim 7, wherein S comprises one or more ~~of the~~ saccharide ~~unit(s) which is (are)~~ selected from the group consisting of glucose, galactose, glucosamine, galactosamine, glucuronic acid, gluconic acid, galacturonic acid, lactose, maltose, maltotriose, isomaltose, isomaltotriose, and neuraminic acid.

9. (Currently Amended) The compound of ~~any one of claims 1 to 8~~ claim 1, wherein the pharmaceutical active compound X is selected from the group consisting of: antibiotic, anti-diabetic, anti-diuretic, anti-cholinergic, anti-arrhythmic, anti-emetic, anti-epileptic, anti-histaminic, anti-mycotic, anti-sympathotonic, anti-thrombotic, androgenic, anti-androgenic, estrogenic, anti-estrogenic, anti-osteoporotic, anti-cancer, immuno-suppressing, vasodilatory antipyretic, analgesic, anti- inflammatory drugs, blood pressure lowering drugs, antitussiva, antidepressiva, β-blockers, and vitamins.

10. (Currently Amended) The compound of ~~any one of claims 1 to 9~~ claim 1, wherein the pharmaceutically active compound X is selected from the group consisting of:

~~a)~~ drugs comprising a primary amino group, ~~preferably selected from the group consisting of:~~

~~Albuterol, Alendronat, Amikazin, Ampicillin, Amoxicillin, Amphotericin B, Atenolol, Azathioprin, Cefaclor, Cefadroxil, Cefotaxim, Ceftazidim, Ceftriaxon, Cilastatin, Cimetidin, Ciprofloxacin, Clonidin, Colistin, Cosyntropin, Cycloserin, Daunorubicin, Doxorubicin, Desmopressin, Dihydroergotamin, Dobutamin, Dopamin, Ephedrin, Epinephrin, ε-Aminocapronsäure, Ergometrin, Esmolol, Famotidin, Flecainid, Folsäure, Flucytosin, Furosemid, Ganciclovir, Gentamicin, Glucagon, Hydrazalin, Imipenem, Isoproterenol, Ketamin, Liothyronin, Merpatricin, Metaraminol, Methyldopa, Metoclopramid, Metoprolol, Mexiletin, Mitomycin, Neomicin, Netilmicin, Nimodipin, Nystatin, Octreotid, Oxytocin, Pamidronat, Pentamidin, Phentolamin, Phenylephrin, Procainamid, Procain, Propranolol, Ritodrin, Sotalol, Teicoplanin, Terbutalin, Thiamin, Tiludronat, Tolazolin, Trimethoprim, Tromethamin, Vancomycin, Vasopressin, and Vinblastin;~~

~~b)~~ drugs comprising a carboxylic acid group, ~~preferably selected from the group consisting of:~~

~~Acetylcystein, Azlocillin, Aztreonam, Benzylpenicillin, Camptothecin, Cefamandol, Cefazolin, Cefepim, Cefotaxim, Cefotetan, Cefoxitin, Ceftazidim, Ceftriaxon, Cephalothin, Cilastatin, Ciprofloxacin, Clavulansäure, Dicloxacillin, ε-Aminocapronsäure, Floxacillin, Folinsäure, Furosemid, Fusidinsaure, Imipemem, Indomethacin, Ketorolac, Liothyronin, Melphalan, Methyldopa, Piperacillin, Prostacyclin, Prostaglandine, Teicoplanin, Ticarcillin and Vancomycin.~~

~~c)~~ drugs comprising an arylic -OH group, ~~preferably selected from the group consisting of:~~

~~Albuterol, Allopurinol, Apomorphin, Ceftriaxon, Dobutamin, Dopamin, Doxycyclin, Edrophonium, Isoproterenol, Liothyronin, Metaraminol, Methyldopa, Minocyclin, Pentazocin, Phenylephrin, Phentolamin, Propofol, Rifamycine, Ritodrin, Teicoplanin, Terbutalin, Tetracyclin and Vancomycin.~~ and

~~d)~~ drugs comprising an aliphatic -OH group, ~~preferably selected from the group consisting of Cyclosporin, Taxol and Paclitaxel~~.

11. (Currently Amended) The compound of ~~any one of claims 1 to 10~~ claim 1, wherein the bifunctional linker is a linker selected from the group consisting of:

~~i)~~ linker molecules that connect an -SH group with an amino group, ~~preferably derived from a compound selected from the group consisting of:~~

~~AMAS (N-α(Maleimidoacetoxy)succinimide ester),~~

~~BMPS (N-β(Maleimidopropyloxy)succinimide ester),~~

~~GMBS (N-γ(Maleimidobutyryloxy)succinimide ester),~~

~~EMCS (N-ε(Maleimidocaproyloxy)succinimide ester),~~

~~MBS (m-Maleimidobenzoyl-N-hydroxysuccinimide ester),~~

~~SMCC (Succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate),~~

~~SMBP (Succinimidyl-4-(p-maleimidophenyl) butyrate),~~

~~SPDP (Succinimidyl-3-(2-pyridyldithio) propionate),~~

~~Sulfo-GMBS (N-(γ-Maleimidobutyryloxy)sulfosuccinimide ester), and~~

~~Sulfo-EMCS (N-(ε-Maleimidocaproyloxy)sulfosuccinimide ester);~~

~~j)~~ linker molecules that connect two -SH groups, ~~preferably derived from a compound selected from the group consisting of:~~

~~BMB (1,4-Bis-maleimidobutane),~~

~~BMDB (1,4-Bis-maleimido-2,3-dihydroxybutane),~~

~~BMH (Bis-maleimidohexane),~~

~~BMOE (Bis-maleimidoethane),~~

~~DTME (Dithio-bis-maleimidoethane),~~

~~HBVS (1,6-Hexane-bis-vinylsulfone),~~

~~$BM(PEO)_3$ (1,8-Bis-maleimidotriethyleneglycol), and~~

~~$BM(PEO)_4$ (1,11-Bis-maleimidotetraethyleneglycol);~~

~~k)~~ linker molecules that connect two amino groups, ~~preferably derived from a compound selected from the group consisting of:~~

~~BSOCOES (Bis-(2-(succinimidyloxycarbonyloxy)-ethyl)sulfone,~~

~~BS^3 (Bis-(sulfosuccinimidyl)-suberate DFDNB (1,5-Difluoro-2,4-dinitrobenzene),~~

~~DMA (Dimethyladipimidate 2HCl),~~

~~DSG (Disuccinimidyl glutarate),~~

~~DSS (Disuccinimidyl suberate), and~~

~~EGS (Ethylene glycol bis(succinimidylsuccinate),~~

~~l)~~ linker molecules that connect an -SH group and a -CHO functional group, ~~preferably derived from a compound selected from the group consisting of:~~

~~BMPH (N-(β-Maleimidopropionic acid)hydrazide TFA),~~

~~EMCH (N-(ε-Maleimidocaproic acid)hydrazide),~~

~~KMUH (N-(κ-Maleimidoundecanoic acid)hydrazide),~~

~~M_2C_2H (4-(N-Maleimidomethyl)cyclohexane-1-carboxylhydrazide HCl),~~

~~MPBH (4-(4-N-Maleimidophenyl)butyric acid hydrazide HCl), and~~

~~PDPH (3-(2-Pyridyldithio)propionyl hydrazide),~~

~~m)~~ linker molecules that connect an -SH group to an -OH group, ~~preferably a compound derived from PMPI (N-(p-Maleimidophenyl)isocyanate);~~

~~n)~~ linker molecules that connect an-SH group to a -COOH group, ~~preferably derived from a compound selected from the group consisting of :~~

~~BMPA (N-β-Maleimidopropionic acid),~~

~~EMCA (N-ε-Maleimidocaproic acid), and~~

~~KMUA (N-κ-Maleimidoundecanoic acid);~~

~~o)~~ linker molecules that transform an amino group into a carboxyl group, ~~preferably derived from a compound selected from the group consisting of : MSA (Methyl-N-succinimidyladipate) and its longer and shorter chain homologues or the corresponding ethylene glycol derivatives;~~ and

~~p)~~ linker molecules that transform a -COOH group into an amino group~~, preferably derived from a compound selected from the group consisting of: DAB (1.4-Diaminobutane) or its longer and shorter chain homologues or the corresponding ethylene glycol derivatives~~.

12. (Currently Amended) A process for preparing compounds according to ~~any one of claims 1,2 and 4 to 11~~ claim 1, comprising the steps of:

a) coupling one or more pharmaceutically active ~~compound(s)~~ compounds X, comprising an amino, alcohol, and/or thiol group, with one or more aldehyde group(s) of S, or

b) coupling one or more pharmaceutical active ~~compound(s)~~ compounds X, comprising an amino, alcohol, and/or thiol group with one or more carboxylic group(s) of S, or

c) coupling one or more pharmaceutical active ~~compound(s)~~ compounds X, comprising an amino, alcohol, and/or thiol group with one or more activated carboxylic group(s) of S, or

d) coupling one or more pharmaceutical active ~~compound(s)~~ compounds X comprising a carboxyl and/or aldehyde functional group with one or more amino, thiol, or alcohol ~~group(s)~~ groups of S.

13. (Previously Presented) The process of claim 12, wherein the coupling in step a) or d) results in the formation of an imine, further comprising the step of reducing the imine to a secondary amine.

14. (Currently Amended) ~~Process~~ The process of claim 12 ~~or 13~~, wherein the imine is reduced by $NaBH_3CN$ at pH values of 6-7.

15. (Currently Amended) The process of ~~any one of claims 12 to 14~~ claim 12, further comprising a step b') or c') prior to step b) or c), respectively, wherein one or more terminal aldehyde ~~group(s)~~ groups of an S precursor are selectively oxidized to produce the S to be used in step b) or c).

16. (Currently Amended) The process of claim 15, wherein the one or more terminal aldehyde ~~group(s)~~ groups of S are selectively oxidized to carboxylic ~~group(s)~~ groups or activated carboxylic ~~group(s)~~ groups using

~~(i)~~ halogen, ~~preferably I_2, Br_2, in alkaline solution, or~~

~~(ii)~~ metal ions, ~~preferably Cu^{++} or Ag^{+}, in alkaline solution,~~ or

(iii) electrochemical oxidation.

17. (Currently Amended) The process of claim 12, wherein in step c) the one or more activated carboxylic ~~group(s)~~ groups of S are activated carboxylic ~~group(s)~~ groups selected from the group consisting of a lactone, an anhydride, a mixed anhydride, and a halogenide of a carboxylic acid.

18. (Currently Amended) The process of claim 12, wherein in step c) the one or more activated carboxylic ~~group(s)~~ groups of S ~~is (are) a~~ are lactone functional ~~group(s)~~ groups.

19. (Currently Amended) The process of claim 17 ~~or 18~~, wherein the coupling of a lactone oligosaccharide derivative and one or more pharmaceutically active ~~compound(s)~~ compounds X comprising an amino function is performed in the absence of an activator.

20. (Currently Amended) The process of ~~claims 18 or 19~~ claim 18, wherein the lactone is coupled in a non-protic ~~solvents, preferably DMF, DMSO, N-methylpyrrolidone,~~ solvent or in an ~~alcohols, preferably MeOH, EtOH, n-PrOH, i-PrOH, n-butanol, iso-butanol, tert-butanol, glycol, glycerol~~ alcohol.

21. (Currently Amended) A process for preparing ~~compounds~~ the compound according to claim 1~~, 3 to 11~~, comprising the steps of:

a) coupling a suitable bifunctional linker group(s) to compound X, and

b) coupling the product(s) of step a) with one or more aldehyde, carboxylic acid, or activated carboxylic group(s) of S, or

a') coupling a suitable bifunctional linker group(s) to one or more aldehyde, carboxylic acid, or activated carboxylic group(s) of S, and

b') coupling the product(s) of step a) with one or more compound(s) X.

22. (CurrentlyAmended) ~~A process according to~~ The process of claim 21, wherein an imine bond that is formed between the bifunctional linker group and the component X and/or S is further reduced to a secondary amine.

23. (Currently Amended) ~~Process~~ The process of claim 22, wherein the imine is reduced by $NaBH_3CN$ at pH values of 6-7.

24. (Currently Amended) The process of claim 21, wherein in step b) or step a') the one or more activated carboxylic ~~group(s)~~ groups of S are activated carboxylic ~~group(s)~~ groups selected from the group consisting of a lactone, an anhydride, a mixed anhydride, and a halogenide of a carboxylic acid.

25. (Currently Amended) The process of ~~claims 21 to 24~~ claim 21, wherein the bifunctional linker comprises a linear or branched aliphatic chain~~, preferably an aliphatic chain~~ of 1 to 20~~, more preferably 1 to 12, most preferably 2 to 6~~ carbon atoms.

26. (Currently Amended) The process of ~~claims 21 to 25~~ claim 21, wherein the bifunctional linker is ~~a linker~~ selected from the group consisting of:

~~i)~~ linker molecules that connect an -SH group with an amino group, ~~preferably derived from a compound selected from the group consisting of:~~

~~AMAS (N-α(Maleimidoacetoxy)succinimide ester),~~

~~BMPS (N-β(Maleimidopropyloxy)succinimide ester),~~

~~GMBS (N-γ(Maleimidobutyryloxy)succinimide ester),~~

~~EMCS (N-ε(Maleimidocaproyloxy)succinimide ester),~~

~~MBS (m-Maleimidobenzoyl-N-hydroxysuccinimide ester),~~

~~SMCC (Succinimidyl-4-(N-maleimidomethyl)-cyclohexane-1-carboxylate),~~

~~SMPB (Succinimidyl-4-(p-maleimidophenyl)-butyrate),~~

~~SPDP (Succinimidyl-3-(2-pyridyldithio)-propionate),~~

~~Sulfo-GMBS (N-(γ-Maleimidobutyryloxy)-sulfosuccinimide ester), and~~

~~Sulfo-EMCS (N-(ε-Maleimidocaproyloxy)sulfosuccinimide ester);~~

~~j)~~ linker molecules that connect two -SH groups, ~~preferably derived from a compound selected from the group consisting of:~~

~~BMB (1,4-Bis-maleimidobutane),~~

~~BMDB (1,4-Bis-maleimido-2,3-dihydroxybutane),~~

~~BMH (Bis-maleimidohexane),~~

~~BMOE (Bis-maleimidoethane),~~

~~DTME (Dithio-bis-maleimidoethane),~~

~~HBVS (1,6-Hexane-bis-vinylsulfone),~~

~~$BM(PEO)_3$ (1,8-Bis-maleimidotriethyleneglycol), and~~

~~$BM(PEO)_4$ (1,11-Bis-maleimidotetraethyleneglycol);~~

~~k)~~ linker molecules that connect two amino groups, ~~preferably derived from a compound selected from the group consisting of:~~

~~BSOCOES (Bis-(2-(succinimidyloxycarbonyloxy)-ethyl) sulfone,~~

~~BS_3 (Bis-(sulfosuccinimidyl)suberateDFDNB (1,5-Difluoro-2,4-dinitrobenzene),~~

~~DMA (Dimethyladipimidate 2HCl),~~

~~DSG (Disuccinimidyl glutarate),~~

~~DSS (Disuccinimidyl suberate), and~~

~~EGS (Ethylene glycol bis(succinimidylsuccinate),~~

~~l)~~ linker molecules that connect an -SH group and a -CHO functional group, ~~preferably derived from a compound selected from the group consisting of:~~

~~BMPH (N-(β-Maleimidopropionic acid)hydrazideTFA),~~

~~EMCH (N-(ε-Maleimidocaproic acid)hydrazide),~~

~~KMUH (N-(κ-Maleimidoundecanoic acid)hydrazide),~~

~~M_2C_2H (4-(N-Maleimidomethyl)cyclohexane-1-carboxylhydrazide HCl),~~

~~MPBH (4-(4-N-Maleimidophenyl)butyric acid hydrazide HCl), and~~

~~PDPH (3-(2-Pyridyidithio)propionyl hydrazide),~~

~~m)~~ linker molecules that connect an -SH group to an -OH group, ~~preferably a compound derived from PMPI (N-(p-Maleimidophenyl)isocyanate);~~

~~n)~~ linker molecules that connect an -SH group to a -COOH group, ~~preferably derived from a compound selected from the group consisting of:~~

~~BMPA (N-β-Maleimidopropionic acid),~~

~~EMCA (N-ε-Maleimidocaproic acid), and~~

~~KMUA (N-κ-Maleimidoundecanoic acid);~~

~~o)~~ linker molecules that transform an amino group into a carboxyl group, ~~preferably derived from a compound selected from the group consisting of: MSA (Methyl-N-~~

~~succinimidyladipate) and its longer and shorter chain homologues or the corresponding ethylene glycol derivatives;~~ and

~~p)~~ linker molecules that transform a -COOH group into an amino group~~, preferably derived from a compound selected from the group consisting of: DAB (1.4-Diaminobutane) or its longer and shorter chain homologues or the corresponding ethylene glycol derivatives~~.

27. (Canceled)

28. (Currently Amended) A pharmaceutical composition comprising ~~at least one of the compounds according to any one of claims 1 to 11~~ the compound of claim 1 and a pharmaceutically active carrier.

29. (Currently Amended) The pharmaceutical composition of claim 28, wherein said composition is freeze-dried. ~~Freeze-dried pharmaceutical composition comprising at least one of the compounds according to any one of claims 1 to 11 and a pharmaceutically active carrier.~~

30. (Currently Amended) A kit comprising ~~at least one of the compounds according to any one of claims 1 to 10~~ the compound of claim 1 in a dehydrated form~~, preferably in~~ or lyophilized form, and at least one physiologically acceptable aqueous solvent.

31. (New) The compound of claim 5, wherein the viscosity of said compound is 1-10 mPasc.

32. (New) The compound of claim 5, wherein the viscosity of said compound 1-7 mPasc.

33. (New) The compound of claim 6, wherein the molar ratio of X to S is in the range of 15:1 to 1:1.

34. (New) The compound of claim 6, wherein the molar ratio of X to S is in the range of 5:1 to 1:1.

35. (New) The compound of claim 6, wherein the molar ratio of X to S is about 1:1.

36. (New) The compound of claim 7, wherein the one or more saccharide units are selected from the group consisting of ribose, arabinose, xylose, lyxose, allose, altrose, glucose, mannose, gulose, idose, galactose, talose, fucose, lactose, maltose, isomaltose, cellobiose, gentiobiose, melibiose, primeverose, rutinose, maltotriose, isomaltotriose, lactotriose, glucuronic acid, galacturonic acid, panose, isopanose, galactosamine, glucosamine, mannosamine, fucosamine, quinovosamine, neuraminic acid, muramic acid, lactosediamine, acosamine, bacillosamine, daunosamine, desosamine, forosamine, garosamine, kanosamine, kansosamine, mycaminose, mycosamine, perosamine, pneumosamine, purpurosamine, rhodosamine, abequose, amicetose, arcanose, ascarylose, boivinose, chacotriose, chalcose,cladinose, colitose, cymarose, 2-deoxyribose, 2-deoxyglucose, diginose, digitalose, digitoxose, evalose, evernitrose,hamamelose, manninotriose,melibiose, mycarose, mycinose, nigerose, noviose, oleandrose, paratose, rhodinose, rutinose, sarmentose, sedoheptulose, solatriose, sophorose, streptose, turanose, and tyvelose.

37. (New) The compound of claim 10, wherein the pharmaceutically active compound X is selected from the group consisting of Albuterol, Alendronat, Amikazin, Ampicillin, Amoxicillin, Amphotericin B, Atenolol, Azathioprin, Cefaclor, Cefadroxil, Cefotaxim, Ceftazidim, Ceftriaxon, Cilastatin, Cimetidin, Ciprofloxacin, Clonidin, Colistin, Cosyntropin, Cycloserin, Daunorubicin, Doxorubicin, Desmopressin, Dihydroergotamin, Dobutamin, Dopamin, Ephedrin, Epinephrin, ε-Aminocaproic acid, Ergometrin, Esmolol, Famotidin, Flecainid, Folic acid, Flucytosin, Furosemid, Ganciclovir, Gentamicin, Glucagon, Hydrazalin, Imipenem, Isoproterenol, Ketamin, Liothyronin, Merpatricin, Metaraminol, Methyldopa, Metoclopramid, Metoprolol, Mexiletin, Mitomycin, Neomicin,

Netilmicin, Nimodipin, Nystatin, Octreotid, Oxytocin, Pamidronat, Pentamidin, Phentolamin, Phenylephrin, Procainamid, Procain, Propranolol, Ritodrin, Sotalol, Teicoplanin, Terbutalin, Thiamin, Tiludronat, Tolazolin, Trimethoprim, Tromethamin, Vancomycin, Vasopressin, Vinblastin, Acetylcystein, Azlocillin, Aztreonam, Benzylpenicillin, Camptothecin, Cefamandol, Cefazolin, Cefepim, Cefotetan, Cefoxitin, Cephalothin, Clavulinic acid, Dicloxacillin, Floxacillin, Folinsäure, Fusidin, Indomethacin, Ketorolac, Melphalan, Piperacillin, Prostacyclin, Prostaglandine, Ticarcillin, Allopurinol, Apomorphin, Doxycyclin, Edrophonium, Minocyclin, Pentazocin, Phentolamin, Propofol, Rifamycine, Tetracyclin, Cyclosporin, Taxol, and Paclitaxel.

38. (New) The compound of claim 11, wherein the bifunctional linker is derived from a compound selected from the group consisting of: N-α(Maleimidoacetoxy)succinimide ester, N-β(Maleimidopropyloxy)succinimide ester, N-γ(Maleimidobutyryloxy)succinimide ester, N-ε(Maleimidocaproyloxy)succinimide ester, m-Maleimidobenzoyl-N-hydroxysuccinimide ester, Succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate, Succinimidyl-4-(p-maleimidophenyl) butyrate, Succinimidyl-3-(2-pyridyldithio) propionate, (N-(γ-Maleimidobutyryloxy)sulfosuccinimide ester, N-(ε-Maleimidocaproyloxy)sulfosuccinimide ester, 1.4-Bis-maleimidobutane, 1.4-Bis-maleimido-2.3-dihydroxybutane, Bis-maleimidohexane, Bis-maleimidoethane, Dithio-bis-maleimidoethane, 1.6-Hexane-bis-vinylsulfone, 1.8-Bis-maleimidotriethyleneglycol, 1.11-Bis-maleimidotetraethyleneglycol, Bis-(2-(succinimidyloxycarbonyloxy)-ethyl)sulfone, Bis-(sulfosuccinimidyl) suberate DFDNB (1.5-Difluoro-2.4-dinitrobenzene, Dimethyladipimidate 2HCl, Disuccinimidyl glutarate, Disuccinimidyl suberate, Ethylene glycol bis(succinimidylsuccinate), N-(β-Maleimidopropionic acid)hydrazide TFA, N-(ε-Maleimidocaproic acid)hydrazide, N-(κ-Maleimidoundecanoic acid)hydrazide, 4-(N-Maleimidomethyl)cyclohexane-1-carboxylhydrazide HCl, 4-(4-N-Maleimidophenyl)butyric acid hydrazide HCl, 3-(2-Pyridyldithio)propionyl hydrazide, N-(p-Maleimidophenyl)isocyanate, N-β-Maleimidopropionic acid, N-ε-Maleimidocaproic acid, N-κ-Maleimidoundecanoic acid, Methyl-N-succinimidyladipate and its longer and

shorter chain homologues or the corresponding ethylene glycol derivatives; and 1.4-Diaminobutane or its longer and shorter chain homologues or the corresponding ethylene glycol derivatives.

39. The process of claim 16, wherein the one or more terminal aldehyde groups of S are selectively oxidized to carboxylic groups or activated carboxylic groups using I_2 or Br_2 in alkaline solution, or Cu^{++} or Ag^{+} in alkaline solution.

40. (New) The process of claim 20, wherein the lactone is coupled in DMF, DMSO, N-methylpyrrolidone, MeOH, EtOH, n-PrOH, i-PrOH, n-butanol, iso-butanol, tert-butanol, glycol, or glycerol.

41. (New) The process of claim 25, wherein the bifunctional linker comprises a linear or branched aliphatic chain of 1 to 12 carbon atoms.

42. (New) The process of claim 25, wherein the bifunctional linker comprises a linear or branched aliphatic chain of 2 to 6 carbon atoms.

43. (New) The process of claim 26, wherein the bifunctional linker is derived from a compound selected from the group consisting of N-α(Maleimidoacetoxy)succinimide ester, N-β(Maleimidopropyloxy)succinimide ester, N-γ(Maleimidobutyryloxy)succinimide ester, N-ε(Maleimidocaproyloxy)succinimide ester, m-Maleimidobenzoyl-N-hydroxysuccinimide ester, Succinimidyl-4-(N-maleimidomethyl)-cyclohexane-1-carboxylate, Succinimidyl-4-(p-maleimidophenyl) butyrate, Succinimidyl-3-(2-pyridyldithio) propionate, N-(γ-Maleimidobutyryloxy) sulfosuccinimide ester), N-(ε-Maleimidocaproyloxy)sulfosuccinimide ester, 1.4-Bis-maleimidobutane, 1.4-Bis-maleimido-2.3-dihydroxybutane, Bis-maleimidohexane, Bis-maleimidoethane, Dithio-bis-maleimidoethane, 1.6-Hexane-bis-vinylsulfone, 1.8-Bis-maleimidotriethyleneglycol, 1.11-Bis-maleimidotetraethyleneglycol, Bis-(2-(succinimidyloxycarbonyloxy)-ethyl) sulfone,

Bis-(sulfosuccinimidyl)suberateDFDNB (1.5-Difluoro-2.4-dinitrobenzene, Dimethyladipimidate 2HCl, Disuccinimidyl glutarate, Disuccinimidyl suberate, Ethylene glycol bis(succinimidylsuccinate, N-(β-Maleimidopropionic acid)hydrazideTFA, N-(ε-Maleimidocaproic acid)hydrazide, N-(κ-Maleimidoundecanoic acid)hydrazide, 4-(N-Maleimidomethyl)cyclohexane-1-carboxylhydrazide HCl, 4-(4-N-Maleimidophenyl)butyric acid hydrazide HCl, and 3-(2-Pyridyidithio)propionyl hydrazide, N-(p-Maleimidophenyl)isocyanate, N-β-Maleimidopropionic acid, N-ε-Maleimidocaproic acid, N-κ-Maleimidoundecanoic acid, Methyl-N-succinimidyladipate and its longer and shorter chain homologues or the corresponding ethylene glycol derivatives, and 1.4-Diaminobutane or its longer and shorter chain homologues or the corresponding ethylene glycol derivatives.